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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,841	02/15/2005	Naoyuki Taniguchi	47234-0003	7031

55694 7590 04/11/2007

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,841	TANIGUCHI ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,23 and 24* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-7 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

Claims 1, 4-7 and 23-24 are pending in the instant Office action.

In response to a previous Office action, a non-final requirement (mailed on June 15, 2006), Applicants have filed an amendment on December 15, 2006, amending claims 1, 4-7, canceling claims 2-3, 8-22, and adding new claim 24. Claim 24, drawn to a an agent for preventing and/or treating arteriosclerosis containing a pharmaceutically effective amount of the peptide or protein as defined in Claim 1 and a pharmaceutically acceptable carrier thereof, is grouped in Group I comprising the same polypeptide. Claim 23, drawn to a method for accelerating neovascularization comprising administering an effective amount of the peptide or the protein of claim 1 to a mammal was withdrawn in the previous Office action as being drawn to non-elected invention. Claim 23 is drawn to a method of accelerating neovascularization by using the polypeptide (elected group) and is grouped under Group V. Examiner regrets that this information was not made clear in the previous Office action.

Therefore, claim 23 remain withdrawn from further consideration as being drawn to non-elected invention.

Claims 1, 4-7 and 24 are under consideration.

Applicants' arguments filed on December 15, 2006 have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Withdrawn-Claim Objections

A previous objection of claims 4 and 7 is withdrawn in view of applicant's amendment to claims and persuasive arguments.

Withdrawn Claim Rejections - 35 U.S.C. § 101

Previous rejection of claims 1, 4-5 under 35 USC § 101, as being non-statutory subject matter is withdrawn in view of Applicant's amendment to claims and persuasive arguments.

Withdrawn Claim Rejections - 35 U.S.C. § 112(2)

Previous rejection of claim 3 under 35 USC § 112, second paragraph, as being indefinite is withdrawn in view of Applicant's cancellation of claim 3.

Previous rejection of claims 6 and 7 under 35 USC § 112, second paragraph, as being indefinite is withdrawn in view of Applicant's amendment to claims and persuasive arguments.

Maintained-Claim Rejections - 35 U.S.C. § 112(2)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Previous rejection of Claim 6 under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained. Claim 6 is indefinite and vague in the recitation of "a neovascularization accelerator", which is ambiguous and confusing. Does it include the presence of anything beyond the polypeptide of claim 1 having neovascularization activity? Applicants argue that the phrase "neovascularization accelerator" is more than adequately set forth in the specification. See, e.g., page 15, lines 13-29 and page 16, lines 1-7. This is not found

persuasive because the specification does not define clearly what the role of said polypeptide/peptide on "neovascularization" process, while the peptide may increase neovascularization, the process itself is a highly complex process and involves the activities of many different polypeptides and peptides. The polypeptide/peptide must have specific activity, which might leads to the acceleration of neovascularization process. Clarification is required.

New Claim Rejections - 35 U.S.C. § 112(2)

Claims 1 and 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 5 are indefinite in the recitation of "an amino acid sequence of SEQ ID NO: 11", which is confusing. Does it include full-length sequence of SEQ ID NO: 11 or partial sequence? Claim 4 is rejected as it depends on claim 1. This rejection can be overcome by stating "the amino acid sequence".

Claims 1 and 4-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is indefinite and vague in the recitation of "neovascularization" in the context of the action of said peptide or polypeptide, which is confusing. The meaning of the term "neovascularization" is clear to the Examiner; however, neovascularization is a complex process, which involves many enzymes or proteins. It is not clear to the Examiner what is the specific role of said peptide or protein without having any specific activity or function rather having a neovascularization action. The Examiner requests clarification.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 24 is indefinite and vague in the recitation of "preventing" in the context of arteriosclerosis by an agent, which is confusing. The term "preventing" or "curing" a disease is very broad term. To claim an agent which can prevent or cure a specific disease needs supporting evidence and working example showing that said agent is indeed capable of preventing or curing a disease. The specification does not provide any evidence that said agent can prevent arteriosclerosis. This rejection can be overcome by deleting the term "preventing".

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 is indefinite and vague in the recitation of a new peptide of "SEQ ID NO: 7", which is not clear to the Examiner. It is not clear to the Examiner whether the polypeptide of claim 5 further comprises SEQ ID NO: 7 or whether SEQ ID NO: 7 takes the position of SEQ ID NO: 11. Furthermore, claim 5 does not further limiting claim 1. Clarification is requested.

Maintained - Claim Rejections - 35 U.S.C. § 112(1st)

Previous rejection of claims 1 and 4-7 and 24 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been described at length in previous

Office Actions. Applicant's amendments to claims 1 and 4-7 and arguments have been fully considered but are not deemed persuasive for the following reasons.

Claims 1, 3-7 and 24 are directed to a genus of any or all peptides or any or all proteins having a neovascularization activity or arteriosclerosis treating activity and containing a basic amino acid cluster region comprising amino acid sequence of SEQ ID NO: 11 or any modified peptide or a protein by modification of one or more amino acids in the amino acid sequence encoded by SEQ ID NO: 7 or an agent for preventing and/or treating arteriosclerosis.

Applicants argue that without acquiescing as to the merit of the rejection as to unamended claim 1, Applicants have amended claim 1 to recite that the basic amino acid cluster region contains at least an amino acid sequence of SEQ ID NO: 11 in addition to previously claimed SEQ ID NO: 7. Applicants also argue that with the amendment, there is sufficient description of the species populating the genus such that a skilled artisan at the time would have understood the meets and bounds of the claim and this particular species is discussed at least in Example 6 of the specification. Applicants request withdrawal of the rejection and allowance of the claims.

Applicant's arguments and amendments to claims have been fully considered but are not deemed to be persuasive to overcome the rejection on Written description issues.

Examiner acknowledges addition of a limitation of the basic amino acid cluster region contains at least an amino acid sequence of SEQ ID NO: 11, however the amendment does not give enough structural feature of any or all peptide or protein having a neovascularization activity, wherein SEQ ID NO: 11 (6 amino acid peptide) is a part of that genus, that is required for fulfilling Written description requirements. As discussed in the written description guidelines

the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient structure and variety of species to reflect the representative structure variation within the genus.** Satisfactory disclosure of a representative structure and number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of species disclosed. For inventions in an unpredictable art, adequate written description of a genus, cannot be achieved by disclosing the structure of small portion of only one species within the genus. The genus of polypeptide having neovascularization activity is structurally diverse as it broadly encompasses mutants, variants and recombinants comprising neovascularization activity having different structures. As such, the disclosure solely of functional features coupled with minor structural feature that may or may not present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus. Therefore, the rejection is maintained.

Previous rejection of Claims 1, 4-7 and 24 under 35 U.S.C. 112, first paragraph on enablement issue is maintained. This rejection has been fully discussed at length in the previous Office action. Applicant's amendments to claims 1 and 4-7 and arguments have been fully considered but are not deemed persuasive for the following reasons.

Claims 1, 4-7 and 24 are so broad as to encompass any or all peptide or any or all proteins having neovascularization activity and comprising a basic amino acid cluster SEQ ID NO: 11 or 7 of any or all peptide or any or all protein from any source or any protein sequence with modification of one or more amino acids or any peptide sequence with modification of one or more amino acids to SEQ ID NO: 7.

Applicants argue that applicants have amended claim 1 to recite that "the basic amino acid cluster region contains at least an amino acid sequence of SEQ ID NO: 11." Applicants also argue that the basic amino acid cluster region containing SEQ ID NO: 11, a skilled artisan at the time would have been enabled to make and use the claimed peptide/proteins and compositions comprising the same. Applicants request withdrawal of the rejection and allowance of the claims.

Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection of claims 1, 4-7 and 24 on enablement issue. The examiner acknowledges the amendment to the claims 1, 4-7 but disagrees with the applicant's contention that the scope of the claimed invention is adequately enabled. Claims 1, 4-7 and 24 are directed to any peptide or any protein having neovascularization activity from any source or any protein sequence with modification of one or more amino acids or any peptide sequence with modification of one or more amino acids to SEQ ID NO: 7. The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins or peptides including mutants and variants having neovascularization activity broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one protein having neovascularization activity (i.e. that encoded by SEQ ID NO: 6).

Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. The specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without affecting neovascularization activity; (B) the general tolerance of protein to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any protein residues with an expectation of obtaining the desired

biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

For all the reasons above, the rejection is maintained.

Withdrawn Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claims 1-4 and 6-7 under 35 U.S.C. 102(b) as being anticipated by Taniguchi et al. (US Patent 5,834,284, publication 11/10/1998, see IDS) is withdrawn in view of applicants amendment of claims and persuasive arguments.

Previous rejection of Claims 1-4 and 6-7 under 35 U.S.C. 102(b) as being anticipated by Taniguchi et al. (EP 0585109 A2, publication 3/2/1994, see IDS) is withdrawn in view of applicants amendment of claims and persuasive arguments.

Maintained- Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claim 5 under 35 U.S.C. 102(b) as being anticipated by Taniguchi

et al. (US Patent 5,834,284, publication 11/10/1998, see IDS) is maintained in view of the recitation of "an amino acid sequence obtained by modification of one or more amino acids in this amino acid sequence". Thus, claim 5 drawn to any protein because one or more amino acids are modified of said protein would result in any protein. Therefore, the protein of Taniguchi et al. anticipates a protein having amino acid sequence of the instant application as written.

New-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-7 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakahara et al. (US Patent 6,191,113 B1, 2/20/2001). Instant claims are drawn to a peptide or protein having a neovascularization action and containing a basic amino acid cluster region wherein the basic amino acid cluster region contains at least an amino acid sequence of SEQ ID NO: 11, wherein the number of basic amino acids accounts for greater than 30% of the total number of amino acids in said region, and a neovascularization accelerator comprising said peptide or protein and a pharmaceutically acceptable carrier or a wound healing agent comprising a pharmaceutically effective amount of said peptide or protein and a pharmaceutically acceptable carrier or an agent for preventing and/or treating arteriosclerosis containing a pharmaceutically effective amount of said peptide or protein and a pharmaceutically acceptable carrier.

Nakahara et al. teach a peptide having 11 amino acids of SEQ ID NO: 11, which is 100% identical (see p8; see sequence alignment) to SEQ ID NO: 11 of the instant application. Nakahara et al. also teach that said peptide having abundant basic amino acids, which is inhibitory to smooth muscle cell proliferation. Nakahara et al. further teach a pharmaceutical composition comprising said peptide which is useful for preventing or treating pathological conditions associated with growth of smooth muscle cells such as arteriosclerosis, restenosis after angioplasty, luminal stenosis after grafting blood vessel and smooth muscle sarcoma (see abstract). Therefore, Nakahara et al. anticipate claim 1, 4-7 and 24 of the instant application.

Claims 1, 4-7 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Selwood et al. (WO 02/34767 A1, publication 5/2/2002). Instant claims are drawn to a peptide or protein having a neovascularization action and containing a basic amino acid cluster region wherein the basic amino acid cluster region contains at least an amino acid sequence of SEQ ID NO: 11, wherein the number of basic amino acids accounts for greater than 30% of the total number of amino acids in said region, and a neovascularization accelerator comprising said peptide or protein and a pharmaceutically acceptable carrier or a wound healing agent comprising a pharmaceutically effective amount of said peptide or protein and a pharmaceutically acceptable carrier or an agent for preventing and/or treating arteriosclerosis containing a pharmaceutically effective amount of said peptide or protein and a pharmaceutically acceptable carrier.

Selwood et al. teach a peptide having 11 amino acids of SEQ ID NO: 10, which is 100% identical (see sequence alignment) to SEQ ID NO: 11 of the instant application. Selwood et al.

also teach that said peptide is from human vascular growth factor (VEGF), wherein said protein is an important signaling protein involved in both vasculogenesis (i.e. *de novo* formation of the embryonic circulatory system) and angiogenesis (the growth of blood vessels from pre-existing vasculature) (see p1, line 4-line 27). Selwood et al. also teach that said peptide has ability to iinhibit angiogenesis. Since Selwood et al. teach a peptide of VEGF of SEQ ID NO: 10, which is 100% identical to SEQ ID NO: 11 having ability to inhibit angiogenesis, therefore, said peptide inherently possesses arteriosclerosis preventing activity. Therefore, Selwood et al. anticipate claim 1, 4-7 and 24 of the instant application.

Claims 1, 4-7 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Tischer et al. (J Biol Chem. 1991 Jun 25; 266(18): 11947-54). Instant claims are drawn to a peptide or protein having a neovascularization action and containing a basic amino acid cluster region wherein the basic amino acid cluster region contains at least an amino acid sequence of SEQ ID NO: 11, wherein the number of basic amino acids accounts for greater than 30% of the total number of amino acids in said region, and a neovascularization accelerator comprising said peptide or protein and a pharmaceutically acceptable carrier or a wound healing agent comprising a pharmaceutically effective amount of said peptide or protein and a pharmaceutically acceptable carrier or an agent for preventing and/or treating arteriosclerosis containing a pharmaceutically effective amount of said peptide or protein and a pharmaceutically acceptable carrier.

Tischer et al. teach a human gene encoding for vascular endothelial growth factor, which is 100% identical (see Fig. 4, amino acid 126 to amino acid 131) to SEQ ID NO: 11 of the instant

application and said protein is an important signaling protein involved in both vasculogenesis (i.e. *de novo* formation of the embryonic circulatory system) and angiogenesis (the growth of blood vessels from pre-existing vasculature). Since Tischer et al. teach a polypeptide for vascular endothelial growth factor, which is 100% identical to SEQ ID NO: 11 of the instant application and said protein is an important signaling protein involved in both vasculogenesis (i.e. *de novo* formation of the embryonic circulatory system) and angiogenesis (the growth of blood vessels from pre-existing vasculature), therefore, said polypeptide or peptide inherently possesses arteriosclerosis preventing activity.

Conclusion

Claims 1, 4-7 and 24 stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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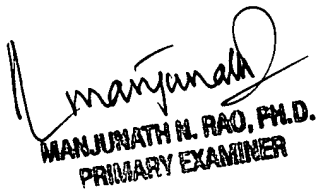

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